

# What is transplant rejection?

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## **Key Points**

- Rejection is damage to a transplant caused by the *body's natural defences*
- Natural defences are *reduced by drugs*, which all kidney transplant patients must take
- A rejection crisis can be treated with extra drugs



## The normal function of the immune system (natural defence)

The usual job of the immune system is to fight invaders into the body. These might be germs or bugs, or foreign objects such as splinters. The body recognises these invaders and tries to eliminate them from the body. The blood not only carries oxygen and nutrients to all parts of the body, but also carries the natural defences to where they are needed in the body. The blood contains two main types of defence system. One is white blood cells which stick to germs and kill them. The other type of defence is antibodies which are smaller than the white blood cells and, by sticking onto germs, either make them burst apart or help the white blood cells to stick to them.

EXHIBIT C (10/719,055)



#### The rejection process

'Rejection' means that someone's body recognises that the transplanted kidney is not 'its own' and tries to 'reject' it from the body. Even when someone is 'well matched' with their transplant kidney (in terms of blood group and tissue type), some degree of rejection is common. The severity of rejection varies from patient to patient. Rejection may be either acute (see below) or chronic (see later). Luckily, there are drugs - called immuno-suppressant drugs (click here for details of drug treatment) - that can help prevent and treat the rejection process.



#### **Acute rejection**

'Acute' means short-term and of rapid onset, requiring immediate action. Acute rejection can occur in the first few months (particularly the first few weeks) after a transplant. It is very common - about 40% of people experience acute rejection in the first three months after a transplant. If acute rejection has not occurred within one year of the operation, then it is unlikely to happen, so long as the anti-rejection drugs are taken regularly.

Acute rejection may sometimes cause pain and fever, but usually there are no symptoms. Doctors will suspect that someone has acute rejection if the blood creatinine is either not coming down after a transplant, or if it has started to fall and then remains stable or increases again. However, acute rejection is not the only reason why there may be problems with blood creatinine levels after a transplant and these other possibilities are usually looked for first.



## Investigation of acute rejection

Tests that might be performed include an ultrasound scan (a sound-wave picture). This will show if the ureter (the tube that takes urine from the kidney to the bladder) is blocked. Other tests use specialist scanning techniques called a radio-isotope scan and a Doppler scan. Either of these will show if there are any problems with the blood supply to the new kidney.

The only way to be sure whether a transplant kidney is being rejected is to do a test called a biopsy. For this test, a hollow needle called a biopsy needle is used to remove a very small piece of the new kidney. This piece of kidney is then looked at under a microscope for any signs of rejection. It is common to have two or more biopsies in

the weeks after the operation.

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### Treatment of acute rejection

If the biopsy shows signs of rejection, then a high-dose steroid drug called methylprednisolone will be given. This drug is usually given by intravenous injection, once a day for three days. These are called 'pulses' of methylprednisolone. Very often, this treatment will suppress the rejection process and the creatinine will start to decrease. Occasionally, someone may need two courses of this drug.

If pulse methylprednisolone does not work, the anti-rejection drugs will be changed to something stronger. The exact changes depend on the severity of rejection and the protocols in different transplant units. If cyclosporin is being used to prevent rejection, it may be changed to tacrolimus ('Prograf') and rejection may subside. Sometimes a five-to-ten-day course of a stronger intravenous drug may be given, such as antilymphocyte globulin (ALG), anti-thymocyte globulin (ATG) or orthoclone K T-cell receptor 3 (OKT3) antibody. These powerful courses of injections have a 70% success rate. All of them can have fairly severe side effects; especially OKT3, which can cause fever, diarrhoea, joint and muscle pain, wheeze, and shortness of breath due to fluid on the lungs (pulmonary oedema).

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# Chronic rejection

'Chronic' means long-term and it starts slowly. The patient's immune system may attack and reject the transplant kidney, but in a different way than in acute rejection.

Chronic rejection looks like a slow ageing of the new kidney. The cause is uncertain. If it happens, it will usually be more than a year after the transplant operation. Doctors may suspect chronic rejection if a patient's blood creatinine starts to rise slowly after it has been stable for some time. As with acute rejection (see above), the only sure way to diagnose the condition is to do a biopsy. There is no treatment for chronic rejection that can be guaranteed to be successful, but some patients get an improvement if the anti-rejection drugs are changed.

The severity of chronic rejection varies. Mild chronic rejection is not usually a problem. However, more severe chronic rejection will eventually lead to failure of the kidney (and therefore to restarting dialysis or having another transplant). Chronic rejection may take years to happen, but it is much the most common cause of transplant failure after the first year.

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The National Kidney Federation cannot accept responsibility for information provided. The above is for guidance only. Patients are advised to seek further information from their own doctor.

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